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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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EXAMINER	
TURNER, SHARON L	
ART UNIT	**PAPER NUMBER**
1647	

DATE MAILED: 05/23/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/015,388	BAKER ET AL.	
	Examiner	Art Unit	
	Sharon L. Turner	1647	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *07 February 2005*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *33,38-40 and 44-54* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *33,38-40 and 44-54* is/are rejected.

7)☒ Claim(s) *33* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *2-7-05*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

Response to Amendment

1. The amendment filed 2-7-05 has been entered into the record and has been fully considered.

2. The text of Title 35 of the U.S. Code not reiterated herein can be found in the previous office action.

3. As a result of Applicant's amendment, all rejections not reiterated herein have been withdrawn.

4. Claims 1-32, 34-37, 41-43 are canceled. Claims 33, 38-40, 44-54 are pending.

Priority

5. Applicant has not complied with one or more conditions for receiving the benefit of an earlier filing date under 35 U.S.C. 119(e), 120 and 365(c) as follows:

The later-filed application must be an application for a patent for an invention which is also disclosed in the prior application (the parent or original nonprovisional application or provisional application); the disclosure of the invention in the parent application and in the later-filed application must be sufficient to comply with the requirements of the first paragraph of 35 U.S.C. 112. See *Transco Products, Inc. v. Performance Contracting, Inc.*, 38 F.3d 551, 32 USPQ2d 1077 (Fed. Cir. 1994).

Applicant's have amended the first line of the specification as directed in the preliminary amendment. The amendment identifies multiple applications upon which priority is claimed. Applicant's have also submitted a priority map that identifies particular applications in which PRO1295 (SEQ ID NO's:53-54) are disclosed.

However, utility is not granted based upon detection in the gene amplification assay as set forth herein. As the priority lineage does not establish compliance with the requirements of 35 USC 112, first paragraph, the effective filing date awarded instant claims is that of the instant filing date, 12-12-01.

Should the Applicant disagree with the Examiner's factual determination above, it is incumbent upon the Applicant to provide the serial number and specific page numbers of any parent application filed prior to12-12-01 which specifically supports the claim limitations for each and every claim limitation in all the pending claims which Applicant considers to have been in possession of and fully enabled for prior to 12-12-01. The utility and enablement of the invention should also be addressed as noted below.

Applicants argue in the 2-7-05 response that they rely on the gene amplification assay disclosed in 60/162,506 for utility and thus are entitled to the 10-29-99 priority date.

Applicants arguments have been fully considered but are not persuasive for the reasons set forth below. The priority documents fail to meet the full requirements of 35 USC 112, and therefore priority is not granted prior to the instant filing date.

Claim Objections

6. Claim 33 is objected to because of the following informalities: the recitation of "in of" which is non-sensical. Also the coding region should be designated via SEQ ID NO: residues such that the public may perceive the portion which is the coding region. The

figure only refers to bolding and underlining of start and stop codons and does not clarify the portion designated via the claim. Appropriate correction is required.

Rejections Maintained or Necessitated by Amendment

Claim Rejections - 35 USC § 101 and § 112

7. 35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

8. Claims 33, 38-40, and 44-54 are rejected under 35 U.S.C. 101 because the claimed invention is not supported by either a specific and substantial asserted utility or a well established utility. Claims 33, 38-40, 44-54 are directed to the nucleic acid of SEQ ID NO: 53 encoding the protein of SEQ ID NO: 54, identified as PRO1295. The instant specification discloses that PRO1295 is a 280 amino acid protein with signal peptide at about residues 1-18. A targeting signal and N-glycosylation site are also noted. The molecular weight is approximates 30,163 daltons with an estimated pI of 6.87. The Figure 32 further identifies that the peptide has the following characteristics; Signal peptide: amino acids 1-18, N-glycosylation site: amino acids 244-248, cAMP- and cGMP-dependent protein kinase phosphorylation site: amino acids 89-93, Casein kinase II phosphoryiation site: amino acids 21-25, 167-171, 223-227, N-myristoylation site: amino acids 100-106, 172-178, 207-213 and Microbodies C-terminal targeting signal: amino acids 278-282. The specification notes homology to various accession numbers but fails to note the specific similarity or the proposed function for PRO1295 or any of the noted homologous segments. The specification further notes testing for the nucleic acid sequence within the gene amplification assay 143 at pp. 506-507 where it

is noted that the PRO 1295 sequence was detected with a change in concentration or doubling within particular (but not all) primary tumor cell lines including lung, colon and breast. No other positive assay is noted for PRO1295.

The specification contains numerous asserted utilities for the polypeptide and encoding nucleic acids, including use as hybridization probes, in chromosome and gene mapping, in the generation of anti-sense RNA and DNA, to identify molecules that bind to PRO (including agonists and antagonists), to make "knock-out" mice or other animals, in gene therapy, as molecular weight markers, therapeutic agents, and for the production of antibodies. However, the utilities that pertain solely to nucleic acids (e.g. hybridization, chromosome and gene mapping, anti-sense) do not convey to the encoded protein. With respect to the remaining utilities, none of these asserted utilities is specific for the disclosed PRO1295 sequence or any activity specifically associated therewith.

The Gene amplification assay is not noted to evidence specific and substantial asserted utility or well established utility because the noted expression is not prescribed to any reasonably likely indication. Given that PRO1295 sequences was amplified in only a very small number of tumors, and not in tumors of the same type, or all tumors, the data do not support the implicit conclusion that the sequences shows positive correlation sufficient to specifically identify lung, colon or breast cancer. Cancerous tissue is known to be aneuploid, that is, having an abnormal number of chromosomes (see Sen, 2000, Curr. Opin. Oncol. 12:82-88). The data presented in the specification were not corrected for aneuploidy. A slight amplification of a gene does not necessarily

mean overexpression in a cancer tissue, but can merely be an indication that the cancer tissue is aneuploid. Even if the data were corrected for aneuploidy, one of ordinary skill in the art would not conclude that PRO1295 would be diagnostic for lung, colon or breast cancer, due to the lack of overexpression in the majority of primary tumor cell types.

Even if the data demonstrated a increase in copy number of PRO1295 nucleic acids in primary tumors, such would not be indicative of a use of the encoded polypeptide as a diagnostic agent. The preliminary data were not supported by analysis of mRNA or protein expression, for example. Also, it does not necessarily follow that an increase in gene copy number results in increased gene expression and increased protein expression, such that the protein would be useful diagnostically or as a target for cancer drug development. For example, Pennica et al. (1998, PNAS USA 95:14717-14722) teach that

> "An analysis of *WISP-1* gene amplification and expression in human colon tumors showed a correlation between DNA amplification and overexpression, whereas overexpression of *WISP-3* RNA was seen in the absence of DNA amplification. In contrast, *WISP-2* DNA was amplified in the colon tumors, but its mRNA expression was significantly reduced in the majority of tumors compared with the expression in normal colonic mucosa from the same patient."

See page 14722, second paragraph of left-hand column; pp.14720-14721; Pages 14720-14721, "Amplification and Aberrant Expression of *WISPs* in Human Colon Tumors". Gygi et al. (Molecular and Cellular Biology, March 1999, p. 1720-1730), studied over 150 proteins relatively homogeneous in half-life and expression level, and found no strong correlation between protein and transcript levels; for some genes, equivalent mRNA levels translated into protein abundances which varied by more than

50-fold. Gygi et al. concluded that the protein levels cannot be accurately predicted from the level of the corresponding mRNA transcript (abstract and Figure 5).

Thus, the data do not support the implicit assertion that the nucleic acids of PRO1295 or the encoded polypeptide can be used as a cancer diagnostic. Significant further research would have been required of the skilled artisan to determine whether PRO1295 is overexpressed in any cancer to the extent that the nucleic acids or polypeptides could be used as a cancer diagnostic, and thus the implicitly asserted utility is not substantial.

Accordingly, while described via SEQ ID NO: structure, the protein and encoding nucleic acids are not evidenced as providing for any specific and substantial asserted utility, or well established utility. No significance or beneifit is prescribed or evidenced for the claimed sequences and their use.

Applicants argue in the response of 2-7-05 that gene amplification is an essential mechanism for oncogene activation, that the gene amp assay is well described, that the results indicate more than a two fold increase in at least 5 tumors (2 primary lung, 2 colon and 1 breast), and that gene amplification occurs in most solid tumors and is associated with poor prognosis. Applicants submit a declaration via Audrey Goddard that states her opinion that the two fold increase in a tumor sample in comparison to normal is useful as a marker for the diagnosis of cancer, for monitoring cancer development and/or for measuring efficacy of cancer therapy. Applicant further argues the declaration evidences TaqMan PCR as a widely recognized, versatile, sensitive and accurate use in gene amplification and that one of skill would find it credible that

PRO1295 is useful as a target for therapeutic intervention in lung colon and breast tumor. Applicants argue that amplification in even 1 tumor sample provides specific and substantial utility as a diagnostic marker of the type of lung or colon tumor in which it was amplified, i.e., amplification would be indicative of that specific class of tumor. Applicants further argue that a declaration via Dr. Avi Ashkenazi explains that as long as a significant difference relative to normal tissue is detected it is irrelevant if the signal originates from aneuploidy and thus is evidence of use as a diagnostic marker.

Applicants arguments filed 2-7-05 have been fully considered but are not persuasive. In particular, the specification shows that PRO1295 showed a two fold increase in 2 primary lung tumors, 2 colon tumor centers and a single breast tumor center out of an undisclosed assortment of primary tumors and cell lines, see Table 8. One skilled in the art would not conclude that such a correlation would indicate that PRO1295 is diagnostic or prognostic for lung, colon, or breast cancer because there is no indication that a majority of any particular cancer type or cancer cell in general exhibit gene amplification of PRO1295 in comparison to other similar and not dissimilar cell types. Applicants submitted references also fail to evidence that such noted increases in expression are useful for diagnostic or prognostic use. In particular Hanna notes column 2, last paragraph that the "clinical significance of such results is unclear." Hyman notes column 1, introduction paragraph 1, that, "the utility of gene expression profiling in the identification of specific therapeutic targets remains limited." Moreover, even Pollack, last line of abstract, notes only that the multiple variations in gene copy number and expression, "may contribute to the development or progression of cancer."

Similarly their conclusion was not one of definitive diagnosis but merely that the CGH analysis provides, "a clearer and more developed understanding of the tumor genome will be forthcoming." No clear diagnostic or prognostic ramifications to particular transcripts or the transcripts of instant claims was prescribed. Moreover, the art recognizes that lung epithelium is at risk for cellular damage due to direct exposure to environmental pollutants and carcinogens, which result in aneuploidy *before* the epithelial cells turn cancerous. See Hittelman (2001, Ann. N. Y. Acad. Sci. 952:1-12), who teach that damaged, *pre-cancerous* lung epithelium is often aneuploid. See especially p. 4, Figure 4. Similarly, aneuploidy was found in morphologically normal colon tissue (Fleischhacker et al., Modern Path., 8:360, 1995; *e.g.,* p. 360, col. 2). Because aneuploid DNA can be found in normal tissues, detection of increased DNA copy number does not necessary mean those cells containing the DNA are cancerous. The gene amplification assay disclosed in the instant specification does not provide a comparison between the lung or colon tumor samples and normal lung, breast or colon epithelium control, and thus it is not clear that PRO1295 is amplified in cancerous lung, breast or colon epithelium more than in damaged (non-cancerous) lung, breast or colon epithelium. Even further there is no indication that the cell lines typified are characterized with respect to vascularization or other morphology which is indicative of progression or metastases and which may all exhibit changes in gene expression that may be non-diagnostic or prognostic in nature. For example, Wu et al., noted that BNF-1, a novel gene encoding a putative extracellular matrix protein is overexpressed in tumor tissues, Gene 311:105-110, 2003. Yet Wu et al., also noted at p.109, paragraph

bridging col. 1-2, that " Interestingly, we observed the up-regulation of BNF-1 not only in breast cancer patients, but also in lung and colon cancer patients, which suggests that the over-expression of BNF-1 is independent of specific tumor type. However, the pathological information provided by commercial companies for these tumor RNAs and cDNAs does not include the vascularized state of the tumor tissues. Nor does it help to clarify the diagnostic or prognostic nature of any over-expressing molecules. Therefore, the relationship between the up-regulation of the BNF-1 in tumor tissues and tumor vascularization is not determined in this study. " Thus, one skilled in the art would not conclude that PRO1295 is a diagnostic probe for lung, breast or colon cancer, nor could they be used to differentiate amongst the variable diagnoses. With respect to the Ashkenazi and Goddard declarations, it is not disputed that tumors may be analyzed for their particular gene expression using the technique of TaqMan PCR. That such is used is evidenced via the noted references. However, the supposition that analysis of any particular cell line with such a technique prescribes based upon changes in particular levels of gene expression immediate diagnostic value to tumor diagnosis is not met by support within the references. No conclusions to diagnostic or prognostic value of the instantly claimed sequences or of sequences overexpreessed in this particular fashion is evidenced. Accordingly, the declarations, while noting probative value for the technique in collecting biological data, fail to evidence patentable utility. Furthermore, the information given in Table 9A was generated using PCR primers that measured amplification of the coding region of SEQ ID NO: 53. However, the claims are broadly drawn to hybridizing fragments and encoding variants which have nucleic

acid substitutions exhibiting an unpredictable effect upon the sequences relation to that of SEQ ID NO:53. One skilled in the art would expect that such variant sequences would lose their specificity as probes for the target sequence. Therefore, even if Applicant were to establish that the gene amplification assay provides utility and enablement for the coding region of SEQ ID NO:53, i.e., as related to the peptide of SEQ NO:54, the utility and enablement would not convey to the claimed encoding portions of degenerate sequences, such variants or to hybridizing fragments. Rejection is maintained.

9. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

10. Claims 33, 38-40, and 44-54 are also rejected under 35 U.S.C. 112, first paragraph. Specifically, since the claimed invention is not supported by either a specific and substantial asserted utility or a well established utility for the reasons set forth above, one skilled in the art clearly would not know how to use the claimed invention. Even if the specification were enabling of how to use the PRO1295 nucleic acids, enablement would not be found commensurate in scope with the claims. If one of skill in the art does not know how to use the nucleic acids or proteins the skilled artisan would clearly not know how to use variable degenerate nucleic acid molecules or nucleic acids that hybridize to a nucleotide sequence encoding the polypeptide.

11. Claims 33, 38-40, and 44-54 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way

as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The specification describes polynucleotides encoding the peptide sequence consisting of SEQ ID NO:54, specifically SEQ ID NO:53 which is shown to test positive in the gene amplification assay as noted above. However, the claims as written include polynucleoitdes encoding the polypeptide of SEQ IDNO:54 and hybridizing fragments. Further, while the specification and claims refer to Figure 32, no definitive direction is provided as to the coding portion of SEQ ID NO:53. Thus, the claims are directed to various generic and sub-generic recitations lacking in identified and correlative structure and function.

However, the instant disclosure of a single polynucleotide encoding a polypeptide, that of SEQ ID NO's :53 and 54, with no disclosed activity, does not adequately support the scope of the claimed genus, which encompasses a substantial variety of subgenera. A genus claim may be supported by a representative number of species as set forth in *Regents of the University of California v Eli Lilly & Co,* 119F3d 1559, 1569, 43 USPQ2d 1398, 1406 (Fed. Cir. 1997), which states:

"To fulfill the written description requirement, a patent specification must describe an invention and do so in sufficient detail that one skilled in the art can clearly conclude that "the inventor invented the claimed invention". Lockwood v. American Airlines, Inc., 107 F.3d 1565, 1572, 41 USPQ2d 1961, 1966 (1997); In re Gosteli, 872 F.2d 1008, 1012, 10 USPQ2d 1614, 1618 (Fed. Cir. 1980) ("[T]he description must clearly allow persons of ordinary skill in the art to recognize that [the inventor] invented what is

claimed.") Thus, an applicant complies with the written description requirement "by describing the invention, with all its claimed limitations, not that which makes it obvious," and by using "such descriptive means as words, structures, figures, diagrams, formulas, etc., that set forth the claimed invention." Lockwood, 107 F.3d 1565, 1572, 41 USPQ2d at 1966.

An adequate written description of a DNA, such as the cDNA of the recombinant plasmids and microorganisms of the '525 patent, "requires a precise definition, such as by structure, formula, chemical name, or physical properties," not a mere wish or plan for obtaining the claimed chemical invention. Fiers v. Revel, 984 F.2d 1164, 1171, 25 USPQ2d 1601, 1606 (Fed. Cir. 1993). Accordingly, "an adequate written description of a DNA requires more than a mere statement that it is part of the invention and reference to a potential method for isolating it; what is required is a description of the DNA itself." Id at 1170, 25 USPQ2d at 1606."

A description of a genus of cDNAs may be achieved by means of a recitation of a representative number of cDNAs, defined by nucleotide sequence, falling within the scope of the genus, or of a recitation of structural features common to the genus, which features constitute a substantial portion of the genus.

However, the instant specification discloses only the single sequences of SEQ ID NO:53 and 54 and no other members of the claimed genus sharing particular function. Given the unpredictability of homology comparisons, see in particular Skolnick et al., Trends in Biotech., 18(1):34-39, 2000 and the fact that the specification fails to provide objective evidence of any additional sequences with the same requisite function, it

cannot be established that a representative number of species have been disclosed to support the genus claim. No activity is set forth for the additional sequences and there is no evidence for a correlation or nexus provided between possession of any homologous feature and any activity as noted such that it is clearly conveyed that possession of any polypeptide having such structural similarity would possess the same function. Thus, the claims lack adequate written description support.

In addition to the aforementioned defects with respect to 112, first paragraph as noted above, the following deficiencies are noted even should utility be found.

Applicants argue in the 2-7-05 response that as utility is provided that the direction in the specification is sufficient to provide adequate written description for the claimed invention.

Applicants arguments filed 2-7-05 have been fully considered but are not persuasive. The utility rejection is maintained as set forth above. Further, with respect to encoding and hybridizing sequences, the variable nucleic acids are not prescribed to the noted increase in expression and therefore the multiple sequences lack description with respect to a common structure and function sufficient to describe a genus. Rejection is therefore maintained.

12. Claims 33, 38-40, and 44-54 are rejected under 35 U.S.C. 112, first paragraph, because the specification does not reasonably provide enablement for the variable encoding and hybridizing sequences and for such generic sequences where no requisite functional activity is provided as claimed. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly

connected, to make and use the invention commensurate in scope with these claims.

The specifications disclosure is insufficient to enable one skilled in the art to practice the invention as broadly claimed without undue experimentation. The factors relevant to this discussion include the quantity of experimentation necessary, the lack of working examples, the unpredictability of the art, the lack of sufficient guidance in the specification and the breadth of the claims.

The skilled artisan readily recognizes that protein chemistry is an unpredictable area of biotechnology. Proteins with replacement of single amino acid residues may lead to both structural and functional changes in biological activity and immunological recognition, see in particular Skolnick et al., Trends in Biotech., 18(1):34-39, 2000. For example, Jobling et al, Mol. Microbiol., 1991, 5(7):1755-67 teaches a panel of single amino acid substitutions by oligonucleotide directed mutagenesis which produce proteins that differ in native conformation, immunological recognition, binding and toxicity, thus exemplifying the importance of conserved structural components to both biological function and immunological recognition.

Instant specification discloses identification of SEQ IDNO:53 in the gene amplification assay but no other activity associated with the structure and function of the molecule that is noted to encode SEQ ID NO:54. However, the specification further fails to note such conserved activities in any variable molecule and fails to teach the significance or use of such modified sequences.

The specification does not enable this broad scope of the claims that encompasses a multitude of analogs or equivalents because the specification does not

teach which residues can or should be modified such that the polynucleotides encoding the polypeptides retain sufficient structural similarity to evoke activity. The specification provides essentially no guidance as to which of the essentially infinite possible choices is likely to be successful and the skilled artisan would not necessarily expect functional conservation among homologous sequences. Moreover, no similar function is required of the additional sequences. The artisan would be unable to determine how to use such similar sequences that lack common function. The additional members would require further experimentation to discover their requisite use. Thus, applicants have not provided sufficient guidance to enable one skilled in the art to make and use the claimed derivatives in a manner reasonably correlated with the scope of the claims.

The scope of the claims must bear a reasonable correlation with the scope of enablement (In re Fisher, 166 USPQ 19 24 (CCPA 1970)). Without such guidance, the changes which can be made and still maintain activity/utility is unpredictable and the experimentation left to those skilled in the art is unnecessarily, and improperly, extensive and undue. See Ex parte Forman, 230 USPQ 546 (Bd. Pat. App. & Int. 1986).

Thus, in view of the quantity of experimentation necessary, the lack of working examples, the unpredictability of the art, the lack of sufficient guidance in the specification and the breadth of the claims the artisan cannot make and use the invention without undue experimentation.

Applicants argue in the 2-7-05 response that as utility is provided that the direction in the specification is sufficient to provide adequate written description for the

claimed invention. Applicants further argue that the experimentation required is not undue with reference to MPEP 2164.01

Applicants arguments filed 2-7-05 have been fully considered but are not persuasive. The utility rejection is maintained as set forth above. Further, with respect to encoding and hybridizing sequences, the variable nucleic acids are not prescribed to the noted increase in expression and therefore the multiple sequences lack enablement with respect to common structure and function sufficient to enable the artisan to make and use the claimed genus. Rejection is therefore maintained.

Claim Rejections - 35 USC § 102

13. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

14. Newly presented claims 48-54 are rejected under 35 U.S.C. 102(b) as being anticipated by GenEmbl Accession No. AC016400, sequencing of chromosome 15 D15S488 region, Ben-Asher, E., et al., Weizman Institute, 26 November 1999.

Accession No. AC016400 teaches a nucleic acid sequence corresponding with 100% similarity to SEQ ID NO:53, residues 1509-2564, a segment of 1056 residues that would inherently and necessarily hybridize given the standard conditions of melting temperatures for annealing nucleic acids including TM=4(G+C)+2(A+T). As the sequences share 100% identity over the segment the would anneal to the

complementary nucleic acids under the noted hybridization conditions. Thus, the reference teachings anticipate the claimed invention.

Conclusion

15. No claims are allowed.

16. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

17. Any inquiry of a general nature or relating to the status of this general application should be directed to the Group receptionist whose telephone number is (703) 308-0196.

Papers relating to this application may be submitted to Technology Center 1600, Group 1640 by facsimile transmission. The faxing of such papers must conform with the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989). Should applicant wish to FAX a response, the current FAX number for Group 1600 is (703) 872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Sharon L. Turner, Ph.D. whose telephone number is (571) 272-0894. The examiner can normally be reached on Monday-Friday from 8:00 AM to 4:30 PM. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Brenda Brumback can be reached at (571) 272-0961.

Sharon L. Turner, Ph.D.
May 10, 2005

SHARON TURNER, PH.D.
PRIMARY EXAMINER
5-10-05